

SUB-ATTACHMENT U-7

DEVELOPMENT OF TISSUE-BASED TOXICITY REFERENCE VALUES

SUB-ATTACHMENT 1

**TARGET TISSUE TOXICITY DATA EXTRACTED FOR TISSUE TRV
DEVELOPMENT**

Table 1.
Summary of References Evaluated to Develop Tissue TRVs for Cadmium

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Doses	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Response Site	Study NOAEL	Study LOAEL	Status	Kidney NOAEL (µg/g, ww)	Kidney LOAEL (µg/g, ww)	Liver NOAEL (µg/g, ww)	Liver LOAEL (µg/g, ww)
Baranski	1983	641	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/0.04/0.4/4.0	mg/kg bw/d	REP	REP	RSEM	WO	4	--	Rejected - Tissue residue not measured	--	--	--	--
Baranski	1983	641	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/0.04/0.4/4.0	mg/kg bw/d	MOR	MOR	SURV	WO	4	--	Rejected - Tissue residue not measured	--	--	--	--
Blakely	1985	547	Cadmium chloride	Mouse (<i>Mus musculus</i>)	4	0/5000/10000/50000	µg/L	GRO	GRO	BDWT	WO	50000	--	Selected for use in TRV development	5.98	--	--	--
Combs	1983	643	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/4.0/7.6/10.1/15.9	µg/g diet	GRO	GRO	BDWT	WO	15.9	--	Selected for use in TRV development	25.05	--	8.35	--
Combs	1983	643	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/4.0/7.6/10.1/15.9	µg/g diet	REP	REP	TEWT	TE	15.9	--	Selected for use in TRV development	25.05	--	8.35	--
Combs	1983	643	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/4.0/7.6/10.1/15.9	µg/g diet	GRO	GRO	BDWT	WO	15.9	--	Selected for use in TRV development	25.05	--	8.35	--
Cousins	1973	502	Cadmium chloride	Pig (<i>Sus scrofa</i>)	5	0/50/150/450/1350	mg/kg diet	GRO	GRO	BDWT	WO	50.0	150	Selected for use in TRV development	41.2	78.4	4.9	8
Cousins	1973	502	Cadmium chloride	Pig (<i>Sus scrofa</i>)	5	0/50/150/450/1350	mg/kg diet	MOR	MOR	WO	1350	--	Selected for use in TRV development	301.4	-	126.6	--	
Cousins	1977	670	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	3	0/5/25	mg/kg diet	GRO	GRO	BDWT	WO	5.00	25.0	Selected for use in TRV development	3.2	20.1	0.5	11.6
Desi	1998	592	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/3.5/7.0/14.0	mg/kg bw/d	REP	REP	PRWT	WO	14.0	--	Rejected - Tissue residue not measured	--	--	--	--
Doyle	1974	3703	Cadmium chloride	Sheep (<i>Ovis aries</i>)	5	0/10.8/29.4/59.7/111.2	mg/org/d	GRO	GRO	BDWT	WO	29.4	59.7	Selected for use in TRV development	187.62	426.81	51.72	62.73
Eakin	1980	659	Cadmium acetate	Rat (<i>Rattus norvegicus</i>)	2	0/150	mg/kg diet	GRO	GRO	BDWT	WO	--	150	Rejected - Tissue concentration presented on a graph	--	--	--	--
Exon	1979	3847	Cadmium acetate	Mouse (<i>Mus musculus</i>)	5	0/30/300/600	mg/L	GRO	GRO	BDWT	WO	300	600	Selected for use in TRV development	76.13	127.92	128.06	282.09
Groten	1991	615	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/30.5	mg/kg diet	GRO	GRO	BDWT	WO	--	30.5	Selected for use in TRV development	--	19.5	--	13.9
Groten	1991	615	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/30.5	mg/kg diet	MOR	MOR	WO	30.5	--	Selected for use in TRV development	19.5	--	13.9	--	
Hamada	1991	465	Cadmium chloride	Dog (<i>Canis familiaris</i>)	6	0/1/3/10/50/100	mg/kg bw/d	GRO	GRO	BDWT	WO	50.0	100	Selected for use in TRV development	135.66	--	--	--
Kajikawa	1981	667	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/L	GRO	GRO	BDWT	WO	--	200	Selected for use in TRV development	--	--	--	--
King	1992	488	Rock phosphate	Pig (<i>Sus scrofa</i>)	3	0/0.60/1.20	mg/kg diet	GRO	GRO	BDWT	WO	1.20	--	Selected for use in TRV development	1.68	--	0.35	--
King	1992	488	Rock phosphate	Pig (<i>Sus scrofa</i>)	5	0/0.47/0.86/2.27/4.46	mg/kg diet	GRO	GRO	BDWT	WO	4.43	--	Selected for use in TRV development	12.25	--	2.01	--
Koller	1977	814	cadmium chloride	Mouse (<i>Mus musculus</i>)	4	0/3/30/300	mg/L	GRO	GRO	BDWT	WO	30.0	300	Selected for use in TRV development	8.35	44.80	--	--
Kotsonis	1978	778	cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/0.41/1.09/2.82	mg/d	REP	REP	PRFM	WO	2.82	--	Rejected - Tissue concentration presented on a graph	--	--	--	--
Lind	1997	685	Cadmium chloride	Mouse (<i>Mus musculus</i>)	2	0/1.24	µg/org/d	GRO	GRO	BDWT	WO	1.24	--	Selected for use in TRV development	0.39	--	0.13	--
Loeser	1977	754	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/1/3/10/30	mg/kg diet	GRO	GRO	BDWT	WO	30.0	--	Rejected - Tissue concentration presented on a graph	--	--	--	--
Loeser	1977	754	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/1/3/10/30	mg/kg diet	REP	REP	SPCL	SM	30.0	--	Rejected - Tissue concentration presented on a graph	--	--	--	--
Mangler	1988	521	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/31.5	mg/L	GRO	GRO	BDWT	WO	31.5	--	Selected for use in TRV development	151.1	--	36.7	--
Mangler	1988	521	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/31.5	mg/L	MOR	MOR	WO	31.5	--	Selected for use in TRV development	151.1	--	36.7	--	
Meyer	1982	662	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/30/60	mg/kg diet	GRO	GRO	BDWT	WO	--	30	Selected for use in TRV development	--	--	--	2.1
Mitra	1995	783	Cadmium	Rat (<i>Rattus norvegicus</i>)	2	0/18.08	µg/q diet	GRO	GRO	BDWT	WO	18.08	--	Rejected - Tissue residue not measured	--	--	--	--
Mitsumori	1998	591	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/8/40/200/600	mg/kg diet	GRO	GRO	BDWT	WO	40.0	200	Rejected - Tissue concentration presented on a graph	--	--	--	--
Ogoshi	1989	720	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	3	0/5/10	mg/L	GRO	GRO	BDWT	WO	5.00	10.0	Rejected - Tissue concentration presented on a graph	--	--	--	--
Ogoshi	1989	720	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	6	0/10/20/40/80/160	mg/L	GRO	GRO	BDWT	WO	80	160	Rejected - Tissue concentration presented on a graph	--	--	--	--
Ogoshi	1989	720	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	3	0/80/160	mg/L	GRO	GRO	MPH	FM	160	--	Rejected - Tissue concentration presented on a graph	--	--	--	--
Perry	1977	3730	Cadmium acetate	Rat (<i>Rattus norvegicus</i>)	7	0/1.2/5.5/10/25/50	mg/L	GRO	GRO	BDWT	WO	10	25	Selected for use in TRV development	65.8	122	28.6	98.3
Pond	1975	3731	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/kg diet	REP	REP	PRWT	WO	--	200	Selected for use in TRV development	--	25.978	--	12.908
Sasser	1985	9321	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/0.69/1.5/2.5	mg/org/d	MOR	MOR	WO	2.50	--	200	Selected for use in TRV development	--	25.978	--	12.908
Sasser	1985	9321	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/0.69/1.5/2.5	mg/org/d	REP	REP	PRWT	WO	1.5	2.5	Selected for use in TRV development	20.0	--	13.4	--
Schroeder	1964	14447	Cadmium	Mouse (<i>Mus musculus</i>)	2	0/5	mg/L	MOR	MOR	SURV	WO	--	5.00	Selected for use in TRV development	--	2.81	--	0.64
Schroeder	1963	14446	Cadmium	Rat (<i>Rattus norvegicus</i>)	2	0/5	mg/L	MOR	MOR	SURV	WO	--	5.00	Selected for use in TRV development	--	4.9	--	--
Schroeder	1963	14446	Cadmium	Rat (<i>Rattus norvegicus</i>)	2	0/5	mg/L	GRO	GRO	BDWT	WO	5	--	Selected for use in TRV development	4.9	--	--	--
Sorell	1990	822	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	4	0/220/1650/2860	µg/org/d	REP	REP	PRWT	WO	220	1650	Selected for use in TRV development	1.66	9.7	0.753	4.16
Steibert	1984	543	cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/50	mg/L	REP	REP	PRWT	WO	--	50.0	Selected for use in TRV development	--	--	--	31.3
Steibert	1984	543	cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/50	mg/L	GRO	GRO	BDWT	WO	50.0	--	Selected for use in TRV development	--	--	29.8	--
Steibert	1984	544	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/50	mg/L	GRO	GRO	BDWT	WO	--	50.0	Selected for use in TRV development	--	62.9	--	--
Steibert	1984	544	Cadmium chloride	Rat (<i>Rattus norvegicus</i>)	2	0/50	mg/L	REP	REP	PRWT	WO	--	50.0	Selected for use in TRV development	--	63.6	--	--
Sugawara	1983</td																	

Table 2.
Summary of References Evaluated to Develop Tissue TRVs for Chromium

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Doses	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Response Site	Study NOAEL	Study LOAEL	Status	Kidney NOAEL (µg/g, ww)	Kidney LOAEL (µg/g, ww)	Liver NOAEL (µg/g, ww)	Liver LOAEL (µg/g, ww)
Anderson	1997	3004	Chromium chloride	Rat (<i>Rattus norvegicus</i>)	5	0/5/25/50/100	mg/kg diet	GRO	GRO	BDWT	WO	100	--	Rejected - Tissue residue not measured	--	--	--	--
Mercado	1973	757	Chromium chloride hexahydrate	Rat (<i>Rattus norvegicus</i>)	2	0/25	mg/L	MOR	MOR	MOR	NR	--	25	Rejected - Tissue residue not measured	--	--	--	--
Mooney	1997	25905	Chromium chloride hexahydrate	Pig (<i>Sus scrofa</i>)	2	0/25200	µg/kg	GRO	GRO	BDWT	WO	25200	--	Rejected - Tissue residue not measured	--	--	--	--
NTP	2008	--	Chromium picolinate monohydrate	Rat (<i>Rattus norvegicus</i>)	4	0/2000/10000/50000	mg/kg diet	GRO	GRO	BDWT	WO	50000	--	Selected for use in TRV development	6.71	--	1.28	--
NTP	2008	--	Chromium picolinate monohydrate	Rat (<i>Rattus norvegicus</i>)	4	0/2000/10000/50000	mg/kg diet	MOR	MOR	MOR	WO	50000	--	Selected for use in TRV development	6.71	--	1.28	--
NTP	2008	--	Chromium picolinate monohydrate	Mouse (<i>Mus musculus</i>)	4	0/2000/10000/50000	mg/kg diet	GRO	GRO	BDWT	WO	50000	--	Selected for use in TRV development	1.20	--	2.90	--
NTP	2008	--	Chromium picolinate monohydrate	Mouse (<i>Mus musculus</i>)	4	0/2000/10000/50000	mg/kg diet	MOR	MOR	MOR	WO	50000	--	Selected for use in TRV development	1.20	--	2.90	--
Schroeder	1963	14446	Trivalent chromium	Rat (<i>Rattus norvegicus</i>)	2	0/5	mg/L	GRO	GRO	BDWT	WO	5	--	Selected for use in TRV development	2.65	--	--	--
Van Heugten	1997	25908	Chromium chloride	Pig (<i>Sus scrofa</i>)	2	0/0.2	mg/kg diet	GRO	GRO	BDWT	WO	0.2	--	Rejected - Tissue residue not measured	--	--	--	--

* See reference section of text for corresponding reference

-- = Not applicable, not available

BDWT = body weight
Conc = concentration

GRO = growth

LOAEL = lowest-observed adverse effects level

mg/kg bw/d = milligrams per kilogram of body weight per day

mg/kg diet = milligrams per kilogram of diet
mg/L = milligrams per liter

MOR = mortality

NOAEL = no-observed adverse effects level

NR = not reported

TRV = Toxicity Reference Value
µg/g = micrograms per gram

µg/kg = micrograms per kilogram

WO = whole organism

ww = wet weight

Table 3.
Summary of References Evaluated to Develop Tissue TRVs for Copper

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Doses	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Response Site	Study NOAEL	Study LOAEL	Kidney NOAEL ($\mu\text{g/g, ww}$)	Kidney LOAEL ($\mu\text{g/g, ww}$)	Liver NOAEL ($\mu\text{g/g, ww}$)	Liver LOAEL ($\mu\text{g/g, ww}$)	
Allcroft	1961	14387	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	4	0/380/560/934	mg/org/d	GRO	GRO	BDWT	WO	560	934	198	307.0	431.3	681.3	
Allcroft	1961	14387	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	4	0/345/579/843	mg/org/d	GRO	GRO	BDWT	WO	843	--	26.8	--	643.8	--	
Allcroft	1961	14387	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	4	0/380/560/934	mg/org/d	MOR	MOR	WO	560	934	198	307.0	431.3	681.3		
Aulerich	1982	2013	Copper sulfate pentahydrate	Mink (<i>Mustela vision</i>)	5	0/25/50/100/200	mg/kg diet	REP	REP	PROG	WO	50	100	--	--	103	91.0	
Aulerich	1982	2013	Copper sulfate pentahydrate	Mink (<i>Mustela vision</i>)	5	0/25/50/100/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	--	--	120	--	
Anugwa	1984	2010	Copper (II) sulfate pentahydrate	Rabbit (<i>Oryctolagus cuniculus</i>)	3	0/122.2/223.67	mg/kg diet	GRO	GRO	BDWT	WO	223.67	--	16.81	--	508.3	--	
Apgar	1995	25922	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	4	0/115/156/242	mg/kg diet	GRO	GRO	BDWT	WO	242	--	12	--	34.5	--	
Arthur	1965	2012	Copper sulfate pentahydrate	Guinea pig (<i>Cavia porcellus</i>)	3	0/10/20	mg/kg diet	GRO	GRO	BDWT	WO	20	--	--	--	14.9	--	
Bailey	2001	25941	Copper sulfate	Cattle (<i>Bos taurus</i>)	3	0/28/55.31	mg/kg diet	GRO	GRO	BDWT	WO	55.31	--	--	--	--	--	
Bassuny	1991	2020	Copper sulfate pentahydrate	Rabbit (<i>Oryctolagus cuniculus</i>)	5	0/75/150/300/450	mg/kg diet	GRO	GRO	BDWT	WO	450	--	--	--	7.5	--	
Bassuny	1991	2020	Copper sulfate pentahydrate	Rabbit (<i>Oryctolagus cuniculus</i>)	5	0/75/150/300/450	mg/kg diet	MOR	MOR	WO	450	--	--	--	--	7.5	--	
Bataineh	1998	1717	Copper chloride dihydrate	Rat (<i>Rattus norvegicus</i>)	2	0/1000	mg/L	REP	REP	TEWT	TE	--	1000	--	--	--	--	--
Boyden	1938	14653	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	5	0/5.1/5.05/8.2/9.8/11.8/7.6	mg/org/d	GRO	GRO	BDWT	WO	--	5.1	--	--	--	64.3	--
Boyden	1938	14653	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	5	0/5.1/5.05/8.2/9.8/11.8/7.6	mg/org/d	MOR	MOR	WO	5.05	7.6	--	--	--	57.0	--	
Braude	1973	2034	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	4	0/147/194/240	mg/kg diet	GRO	GRO	BDWT	WO	240	--	--	--	--	71.643	--
Bush	1995	2043	Copper sulfate pentahydrate	Mink (<i>Mustela vision</i>)	3	0/308/568	mg/kg diet	GRO	GRO	BDWT	WO	568	--	4.4	--	44.6	--	
Bush	1995	2043	Copper sulfate pentahydrate	Mink (<i>Mustela vision</i>)	3	0/308/568	mg/kg diet	MOR	MOR	WO	568	--	4.4	--	44.6	--		
Cromwell	1989	2061	Copper oxide	Pig (<i>Sus scrofa</i>)	3	0/125/250	mg/kg diet	GRO	GRO	BDWT	WO	250	--	--	--	--	6.3	--
Cromwell	1989	2061	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	3	0/125/250	mg/kg diet	GRO	GRO	BDWT	WO	250	--	--	--	--	61.5	--
Cromwell	1989	2061	Copper sulfate	Pig (<i>Sus scrofa</i>)	5	0/125/250/375/550	mg/kg diet	GRO	GRO	BDWT	WO	550	--	--	--	--	378.3	--
Cromwell	1989	2061	Copper oxide	Pig (<i>Sus scrofa</i>)	4	0/125/250/500	mg/kg diet	GRO	GRO	BDWT	WO	500	--	--	--	--	5.3	--
Cromwell	1989	2061	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	4	0/125/250/500	mg/kg diet	GRO	GRO	BDWT	WO	500	--	--	--	--	81.8	--
Cromwell	1993	2062	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	REP	REP	RSUC	WO	--	250	--	14.8	--	474.8	--
Cromwell	1993	2062	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	GRO	GRO	BDWT	WO	250	--	14.8	--	474.8	--	
Cromwell	1993	2062	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	MOR	MOR	MOR	WO	250	--	14.8	--	474.8	--	
Cromwell	1998	25930	Copper chloride	Pig (<i>Sus scrofa</i>)	4	0/100/150/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	--	--	--	--	--
Cromwell	1998	25930	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	--	--	--	--	--
Cromwell	1998	25930	Copper chloride - tribasic	Pig (<i>Sus scrofa</i>)	2	0/116/218	mg/kg diet	GRO	GRO	BDWT	WO	218	--	--	--	--	21	--
Cromwell	1998	25930	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/231	mg/kg diet	GRO	GRO	BDWT	WO	231	--	--	--	--	24	--
Cromwell	1998	25930	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	3	0/117/226	mg/kg diet	GRO	GRO	BDWT	WO	226	--	--	--	--	31.8	--
Cromwell	1998	25930	Copper chloride	Pig (<i>Sus scrofa</i>)	4	0/124/167/241	mg/kg diet	GRO	GRO	BDWT	WO	241	--	--	--	--	22	--
DeGoey	1971	2064	Copper sulfate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	GRO	GRO	BDWT	WO	--	250	--	--	--	41.8	--
DeGoey	1971	2064	Copper sulfate	Pig (<i>Sus scrofa</i>)	2	0/500	mg/kg diet	GRO	MPH	MUSC	MU	--	500	--	--	--	414.0	--
DeGoey	1971	2064	Copper sulfate	Pig (<i>Sus scrofa</i>)	2	0/500	mg/kg diet	MOR	MOR	MOR	WO	--	500	--	--	--	414.0	--
Devries	1986	10891	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/12	mg/org/d	GRO	GRO	BDWT	WO	12	--	--	--	--	27.8	--
Edmonds	1986	2075	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	3	0/250/650	mg/kg diet	GRO	GRO	BDWT	WO	250	650	--	--	--	62.88	516.28
Edmonds	1986	2075	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	3	0/250/650	mg/kg diet	MOR	MOR	MOR	WO	650	--	--	--	--	516.28	--
Engle	2001	25940	Copper sulfate	Cattle (<i>Bos taurus</i>)	2	0/40	mg/kg diet	GRO	GRO	BDWT	WO	40	--	--	--	--	89.0	--
Engle	2000	25935	Copper chloride - tribasic	Cattle (<i>Bos taurus</i>)	2	0/40	mg/kg diet	GRO	GRO	BDWT	WO	40	--	--	--	--	127.5	--
Felsman	1973	3760	Copper sulfate	Cattle (<i>Bos taurus</i>)	4	0/125/250/500	mg/kg diet	GRO	GRO	BDWT	WO	500	--	--	--	--	230	--
Felsman	1973	3760	Copper sulfate	Cattle (<i>Bos taurus</i>)	4	0/300/600/900	mg/kg diet	GRO	GRO	BDWT	WO	900	--	--	--	--	205	--
Fuentelba	2000	36364	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/1500	mg/kg diet	GRO	GRO	BDWT	WO	--	1500	--	--	--	1603	--
Gershbein	1983	136	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	2	0/75	mg/kg diet	GRO	GRO	BDWT	WO	75	--	--	--	--	--	--
Gipp	1973	14396	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	GRO	GRO	BDWT	WO	250	--	--	--	--	340.6	--
Gipp	1974	14397	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	GRO	GRO	BDWT	WO	250	--	32.5	--	1520	--	
Gopinath	1974	36202	Copper sulfate pentahydrate	Sheep (<i>Ovis aries</i>)	2	0/20	mg/kg bw/d	MOR	MOR	WO	--	20	--	136.85	--	--	--	
Grobner	1986	2113	Anhydrous Copper sulfate	Rabbit (<i>Oryctolagus cuniculus</i>)	6	0/55.9/121.5/199.2/498.1/821.6	mg/kg diet</td											

Table 3.
Summary of References Evaluated to Develop Tissue TRVs for Copper

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Doses	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Response Site	Study NOAEL	Study LOAEL	Kidney NOAEL (µg/g, ww)	Kidney LOAEL (µg/g, ww)	Liver NOAEL (µg/g, ww)	Liver LOAEL (µg/g, ww)
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	REP	REP	SPCL	SM	8000	--	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	GRO	GRO	BDWT	WO	4000	8000	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	GRO	GRO	BDWT	WO	4000	8000	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	GRO	GRO	BDWT	WO	16000	--	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	MOR	MOR	MOR	WO	16000	--	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	MOR	MOR	MOR	WO	16000	--	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/1000/2000/4000/8000/16000	mg/kg diet	MOR	MOR	MOR	WO	16000	--	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/300/1000/3000/10000/30000	mg/L	GRO	GRO	BDWT	WO	1000	3000	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/300/1000/3000/10000/30000	mg/L	GRO	GRO	BDWT	WO	1000	3000	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/300/1000/3000/10000/30000	mg/L	MOR	MOR	MOR	WO	3000	10000	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Mouse (<i>Mus musculus</i>)	6	0/300/1000/3000/10000/30000	mg/L	MOR	MOR	MOR	WO	1000	3000	--	--	--	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/500/1000/2000/4000/8000	mg/kg diet	REP	REP	SPCL	SM	8000	--	181.03	--	372.12	--
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/500/1000/2000/4000/8000	mg/kg diet	GRO	GRO	BDWT	WO	4000	8000	52.89	181.03	127.31	372.12
Hebert	1993	2126	Copper (II) sulfate pentahydrate	Rat (<i>Rattus norvegicus</i>)	6	0/500/1000/2000/4000/8000	mg/kg diet	MOR	MOR	MOR	WO	8000	--	181.03	--	372.12	-
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	4	0/32/129/259	mg/org/d	REP	REP	SPCL	SM	259	--	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	4	0/173/736/3201	mg/org/d	REP	REP	SPCL	SM	3201	--	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	6	0/32/64/129/259/551	mg/org/d	GRO	GRO	BDWT	WO	129	259	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	5	0/41/113/175/140	mg/org/d	GRO	GRO	BDWT	WO	113	175	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	6	0/92/180/363/777/1275	mg/org/d	GRO	GRO	BDWT	WO	363	777	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	5	0/41/95/226/524	mg/org/d	GRO	GRO	BDWT	WO	95	226	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	6	0/173/382/736/1563/3201	mg/org/d	GRO	GRO	BDWT	WO	173	382	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	6	0/168/362/773/1154/2817	mg/org/d	GRO	GRO	BDWT	WO	1154	2817	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	5	0/41/113/175/140	mg/org/d	MOR	MOR	MOR	WO	113	175	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	6	0/32/64/129/259/551	mg/org/d	MOR	MOR	MOR	WO	551	--	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	5	0/41/95/226/524	mg/org/d	MOR	MOR	MOR	WO	95	226	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	6	0/92/180/363/777/1275	mg/org/d	MOR	MOR	MOR	WO	1275	--	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	6	0/168/362/773/1154/2817	mg/org/d	MOR	MOR	MOR	WO	2817	--	--	--	--	--
Hebert	1993	2127	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	6	0/173/382/736/1563/3201	mg/org/d	MOR	MOR	MOR	WO	3201	--	--	--	--	--
Ishmael	1971	2155	Copper sulfate pentahydrate	Sheep (<i>Ovis aries</i>)	2	0/0.714	g/org/d	MOR	MOR	MOR	WO	--	0.714	--	72.18	--	432.58
Jenkins	1989	48117	Copper	Cattle (<i>Bos taurus</i>)	5	0/50/200/500/1000	mg/kg diet	MOR	MOR	MOR	WO	500	1000	--	--	--	963.8
Keen	1982	11928	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	4	0/100/1000/2000	µg/g diet	GRO	GRO	BDWT	WO	1000	2000	--	--	66.8	602.6
Keen	1982	11928	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	4	0/100/1000/2000	µg/g diet	MOR	MOR	MOR	WO	1000	2000	--	--	66.8	602.6
King	1975	2179	copper sulfate pentahydrate	Rabbit (<i>Oryctolagus cuniculus</i>)	2	0/100	mg/kg diet	GRO	GRO	BDWT	WO	100	--	--	--	--	--
King	1975	2179	copper sulfate pentahydrate	Rabbit (<i>Oryctolagus cuniculus</i>)	2	0/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	--	--	--	--
Kline	1971	20975	Copper sulfate	Pig (<i>Sus scrofa</i>)	4	0/151/197/246	mg/kg diet	GRO	GRO	BDWT	WO	246	--	--	--	36.8	--
Komulainen	1983	12079	Copper chloride	Rat (<i>Rattus norvegicus</i>)	4	0/28/50/64	mg/kg bw/d	GRO	GRO	BDWT	WO	50	64	--	--	--	--
Kumar	1987	2186	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/0.1	g/kg bw/d	GRO	GRO	BDWT	WO	--	0.1	--	5.113	--	--
Lalich	1965	2189	Copper (II) sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/0.5	g/kg diet	GRO	GRO	BDWT	WO	0.5	--	--	--	--	--
Lecyk	1980	2193	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	7	0/0/5/1.0/1.5/2.0/3.0/4.0	g/kg diet	REP	REP	PROG	WO	2	3	--	--	--	--
Lecyk	1980	2193	Copper (II) sulfate	Mouse (<i>Mus musculus</i>)	7	0/0.5/1.0/1.5/2.0/3.0/4.0	g/kg diet	REP	REP	PROG	WO	2	3	--	--	--	--
Llewellyn	1985	2203	Copper acetate	Rat (<i>Rattus norvegicus</i>)	2	0/2600	mg/kg diet	GRO	GRO	BDWT	WO	--	2600	--	--	--	--
Luo	1996	25929	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	GRO	GRO	BDWT	WO	250	--	14.6	--	123	--
McNatt	1971	2216	Copper (I) acetate	Rat (<i>Rattus norvegicus</i>)	2	0/0.2	% in diet	MOR	MOR	MOR	WO	--	0.2	--	--	--	213
Miranda	1981	36240	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/55.1	µg/g diet	GRO	GRO	BDWT	WO	55.1	--	--	--	67.1	--
Myers	1993	2225	Copper (I) acetate	Rat (<i>Rattus norvegicus</i>)	2	0/0.125	% in diet	GRO	GRO	BDWT	WO	0.125	--	--	--	39.03	--
Myres	1973	12809	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/250											

Table 3.
Summary of References Evaluated to Develop Tissue TRVs for Copper

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Doses	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Response Site	Study NOAEL	Study LOAEL	Kidney NOAEL ($\mu\text{g/g}$, ww)	Kidney LOAEL ($\mu\text{g/g}$, ww)	Liver NOAEL ($\mu\text{g/g}$, ww)	Liver LOAEL ($\mu\text{g/g}$, ww)
Smith	1975	3756	Cupric carbonate	Horse - Shetland pony (<i>Equus caballus</i>)	4	0/691.7/1209.1/2088.2	mg/org/d	GRO	GRO	BDWT	WO	2088.2	--	--	--	209	--
Solaiman	2001	36748	Copper sulfate pentahydrate	Goat (<i>Capra hircus</i>)	3	0/50/100	mg/org/d	GRO	GRO	BDWT	WO	--	50	--	--	--	--
Suttle	1966	3757	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	3	0/250/425	mg/kg diet	GRO	GRO	BDWT	WO	250	425	--	--	520.0	692.5
Tatum	2000	36389	Copper chloride	Rat (<i>Rattus norvegicus</i>)	2	0/800	mg/kg diet	GRO	GRO	BDWT	WO	800	--	--	--	78	--
Thacker	1991	2304	Copper sulfate	Pig (<i>Sus scrofa</i>)	2	0/250	mg/kg diet	REP	REP	PROG	WO	250	--	--	--	--	--
Uthus	2001	36349	Cupric carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/25	$\mu\text{g/g}$ diet	GRO	GRO	BDWT	WO	25	--	9.25	--	4	--
Ward	1991	1888	Copper sulfate pentahydrate	Pig (<i>Sus scrofa</i>)	2	0/199	mg/kg diet	GRO	GRO	BDWT	WO	199	--	--	--	95.0	--
White	1985	2324	Copper sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/500	mg/kg diet	GRO	GRO	BDWT	WO	500	--	--	--	5.3	--

* See reference section of text for corresponding reference

-- = Not applicable, not available

% in diet = percent in diet

BDWT = body weight

Conc = concentration

g/kg bw/d = grams per kilogram per body weight per day

g/kg diet = grams per kilogram of diet

g/org/d = grams per organism per day

GRO = growth

LOAEL = lowest-observed adverse effects level

mg/kg bw/d = milligrams per kilogram of body weight per day

mg/kg diet = milligrams per kilogram of diet

mg/org/d = milligrams per organism per day

MOR = mortality

mg/L = milligrams per liter

MPH = morphology

MU = muscle

MUSC = muscle changes

NOAEL = no-observed adverse effects level

PROG = progeny counts/numbers

REP = reproduction

RSUC = reproductive success (general)

SM = sperm

SPCL = sperm cell counts

TE = testes

TEWT = testes weight

TRV = Toxicity Reference Value

$\mu\text{g/g}$ = micrograms per gram

$\mu\text{g/g}$ diet = micrograms per gram of diet

WO = whole organism

ww = wet weight

Table 4.
Summary of References Evaluated to Develop Tissue TRVs for Lead

Primary Author	Year	Reference ID*	Chemical Form	Test Species	Conc/Dose s	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Respons e Site	Study NOAEL	Study LOAEL	Status	Kidney NOAEL (µg/g, ww)	Kidney LOAEL (µg/g, ww)	Liver NOAEL (µg/g, ww)	Liver LOAEL (µg/g, ww)
Azar	1973	3747	Lead acetate	Rat (<i>Rattus norvegicus</i>)	5	0/18/62/141/548	mg/kg diet	MOR	MOR	WO	141	548	Selected for use in TRV development	2.31	13.2	0.6	1.87	
Azar	1973	3747	Lead acetate	Dog (<i>Canis familiaris</i>)	5	0/16/57/155/576	mg/kg diet	MOR	MOR	WO	576	--	Selected for use in TRV development	2.91	--	7.89	--	
Azar	1973	3747	Lead acetate	Rat (<i>Rattus norvegicus</i>)	3	0/1130/2102	mg/kg diet	MOR	MOR	WO	1130	2102	Selected for use in TRV development	--	--	1.87	2.8	
Bankowska	1985	14852	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/350	mg/L	GRO	GRO	BDWT	WO	350	--	Selected for use in TRV development	27.5	--	3.22	--
Bankowska	1985	14852	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/350	mg/L	MOR	MOR	WO	350	--	Selected for use in TRV development	12.8	--	3.12	--	
Barlow	1977	2523	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/2	% in diet	REP	REP	PRWT	WO	--	2.00	Selected for use in TRV development	--	--	9	--
Barlow	1977	2523	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/2	% in diet	GRO	GRO	BDWT	WO	--	2.00	Selected for use in TRV development	--	--	9	--
Batra	1998	2528	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/50	mg/kg bw/d	REP	REP	TEDG	TE	--	50.0	Selected for use in TRV development	--	2,052	--	0.9111
Blanusa	1981	14750	Lead acetate	Rat (<i>Rattus norvegicus</i>)	5	0/1500/3500/5500/7500	mg/L	REP	REP	RHIS	WO	--	1500	Selected for use in TRV development	--	25.2	--	--
Brady	1975	14795	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/240	mg/org	REP	REP	PRWT	WO	240	--	Rejected - No tissue data presented	--	--	--	--
Brady	1975	14795	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/240	mg/org	GRO	GRO	BDWT	WO	240	--	Rejected - No tissue data presented	--	--	--	--
Cerklewski	1980	10607	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/250	mg/kg diet	REP	REP	PRWT	WO	250	--	Rejected - Tissue data presented on graph	--	--	--	--
Cernochova	1992	2568	Lead dinitrate	Mouse (<i>Mus musculus</i>)	2	0/21.75	mg/org	REP	REP	TEDG	TE	--	0.614	Rejected - No tissue data presented	--	--	--	--
Dilts	1980	2592	Lead acetate	Rat (<i>Rattus norvegicus</i>)	6	0/10/50/100/200/500	mg/L	REP	REP	PRWT	WO	50.0	100	Rejected - No tissue data presented	--	--	--	--
Dilts	1979	2593	Lead acetate	Rat (<i>Rattus norvegicus</i>)	6	0/10/50/100/200/500	mg/L	REP	REP	PRWT	WO	10.0	50.0	Rejected - No tissue data presented	--	--	--	--
Dilts	1979	2593	Lead acetate	Rat (<i>Rattus norvegicus</i>)	6	0/10/50/100/200/500	mg/L	GRO	GRO	BDWT	WO	10.0	50.0	Rejected - No tissue data presented	--	--	--	--
Donald	1981	2598	Lead acetate	Mouse (<i>Mus musculus</i>)	2	0/0.13	% in water	REP	REP	PRWT	WO	--	0.130	Rejected - Tissue data not associated with dosed organism	--	--	--	--
El-Gazzar	1978	21143	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/100	mg/L	GRO	GRO	BDWT	WO	100	--	Selected for use in TRV development	1.95	--	0.64	--
Exon	1979	3847	Lead acetate	Mouse (<i>Mus musculus</i>)	5	0/13/130/1300/2600	mg/L	GRO	GRO	BDWT	WO	2600	--	Selected for use in TRV development	46.68	--	11.2	--
Fick	1976	3704	Lead acetate	Sheep (<i>Ovis aries</i>)	5	0/10/100/500/1000	mg/kg diet	GRO	GRO	BDWT	WO	1000	--	Selected for use in TRV development	57.65	--	3.60	--
Fox	1977	2633	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/1092	mg/L	REP	REP	PRWT	WO	1092	--	Rejected - No tissue data presented	--	--	--	--
Fox	1982	2634	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/0.5	µg/g bw/d	GRO	GRO	BDWT	WO	0.500	--	Rejected - No tissue data presented	--	--	--	--
Gandley	1999	2642	Lead acetate	Rat (<i>Rattus norvegicus</i>)	3	0/25/250	mg/L	REP	REP	RSUC	WO	25.0	250	Rejected - No tissue data presented	--	--	--	--
Goyer	1970	14799	Lead acetate	Rat (<i>Rattus norvegicus</i>)	6	0/2.3/7.0/12/21/67/220	mg/org/d	GRO	GRO	BDWT	WO	21.0	67.0	Selected for use in TRV development	30.4	36.6	--	--
Gupta	1995	2666	Lead acetate	Mouse (<i>Mus musculus</i>)	4	0/10/25/50	mg/kg bw	REP	REP	PROG	EM	--	10.0	Selected for use in TRV development	--	1	--	--
Harry	1985	2680	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/kg bw	GRO	GRO	BDWT	WO	--	200	Selected for use in TRV development	--	18.49	--	9.655
Hayashi	1983	3864	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/500	mg/L	REP	REP	PRWT	WO	--	500	Selected for use in TRV development	--	--	--	1.59
Hsu	1980	2704	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/0.5	% in diet	REP	REP	PRWT	WO	--	0.500	Rejected - No tissue data presented	--	--	--	--
Hsu	1975	14376	Lead acetate	Pig (<i>Sus scrofa</i>)	2	0/1000	mg/L	GRO	GRO	BDWT	WO	--	1000	Selected for use in TRV development	--	15	--	39.8
Jessup	1967	2720	Lead acetate	Rabbit (<i>Oryctolagus cuniculus</i>)	3	0/54.6/546	mg/kg diet	MOR	MOR	WO	546	--	Rejected - No tissue data presented	--	--	--	--	
Jessup	1969	2721	Lead acetate	Rat (<i>Rattus norvegicus</i>)	4	0/10/100/1000	mg/kg diet	MOR	MOR	SURV	WO	1000	--	Could not locate article	--	--	--	--
Johansson	1986	2723	Lead chloride	Mouse (<i>Mus musculus</i>)	2	0/1	g/L	REP	REP	PRFM	WO	--	1.00	Rejected - No tissue data presented	--	--	--	--
Johansson	1986	2723	Lead chloride	Mouse (<i>Mus musculus</i>)	2	0/1	g/L	GRO	GRO	BDWT	WO	1.00	--	Rejected - No tissue data presented	--	--	--	--
Kishi	1983	12025	Lead acetate	Rat (<i>Rattus norvegicus</i>)	4	0/45/90/180	mg/kg bw	GRO	GRO	BDWT	WO	180	--	Selected for use in TRV development	9.45	--	4.63	--
Krigman	1974	2741	Lead carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/4	% in diet	REP	REP	PRWT	WO	--	4.00	Selected for use in TRV development	--	10	--	4.6
Logner	1984	3889	Lead sulfate	Cattle (<i>Bos taurus</i>)	4	0/16/43/305	mg/kg bw/d	GRO	GRO	BDWT	WO	43.0	--	Selected for use in TRV development	5.320	--	4.170	--
Logner	1984	3889	Lead sulfate	Cattle (<i>Bos taurus</i>)	4	0/16/43/305	mg/kg bw/d	MOR	MOR	WO	16.0	43.0	Selected for use in TRV development	1.82	5.32	1.67	4.17	
Lorenzo	1978	2751	Lead nitrate	Rabbit (<i>Oryctolagus cuniculus</i>)	3	0/10/7.50.4	mg/kg bw/d	GRO	GRO	BDWT	WO	10.7	50.40	Rejected - No tissue data presented	--	--	--	--
Lorenzo	1978	2751	Lead nitrate	Rabbit (<i>Oryctolagus cuniculus</i>)	5	0/10/7.50.4	mg/kg bw/d	MOR	MOR	WO	10.7	50.4	Rejected - No tissue data presented	--	--	--	--	
Mahaffey	1973	2756	Lead acetate	Rat (<i>Rattus norvegicus</i>)	7	0/0.19/0.70/2.8/5.9/12.9/24.3	mg/kg bw/d	GRO	GRO	BDWT	WO	24.3	--	Selected for use in TRV development	20.4	--	--	--
Mahaffey	1977	14580	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	Rejected - No tissue data presented	--	--	--	--
McMurry	1995	2770	Lead acetate	Cotton rat (<i>Sigmodon hispidus</i>)	3	0/21/28.8	mg/org	REP	REP	RHIS	RT	2.10	28.8	Rejected - No tissue data presented	--	--	--	--
Miller	1982	2775	Lead acetate	Rat (<i>Rattus norvegicus</i>)	4	0/50/75/100	mg/kg bw	REP	REP	PRWT	WO	75.0	100	Selected for use in TRV development	5.648	6.550	0.643	0.908
Morris	1938	15125	Lead acetate	Rat (<i>Rattus norvegicus</i>)	3	0/1269/9307.8	µg/org/d	REP	REP	PRWT	WO	--	1269	Rejected - Tissue data not associated with dosed organism	--	--	--	--
Morris	1938	15125	Lead acetate	Rat (<i>Rattus norvegicus</i>)	3	0/1269/9307.8	µg/org/d	GRO	GRO	BDWT	WO	9308	--	Rejected - Tissue data not associated with dosed organism	--	--	--	--

Table 4.
Summary of References Evaluated to Develop Tissue TRVs for Lead

Primary Author	Year	Reference ID*	Chemical Form	Test Species	Conc/Dose s	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Respon s e Site	Study NOAEL	Study LOAEL	Status	Kidney NOAEL (µg/g, ww)	Kidney LOAEL (µg/g, ww)	Liver NOAEL (µg/g, ww)	Liver LOAEL (µg/g, ww)
White	1977	2929	Lead carbonate	Dog (<i>Canis familiaris</i>)	2	0/50	mg/kg bw	GRO	GRO	BDWT	WO	--	50	Rejected - No tissue data presented	--	--	--	--
Wiebe	1988	2930	Lead chloride	Rat (<i>Rattus norvegicus</i>)	3	0/20/200	mg/kg	GRO	GRO	BDWT	WO	20.0	--	Selected for use in TRV development	0.55	--	--	--
Willoughby	1972	14386	Lead carbonate	Horse (<i>Equus caballus</i>)	2	0/30	mg/kg diet	GRO	GRO	BDWT	WO	30.0	--	Selected for use in TRV development	0.4	--	1.35	--
Yagminas	1990	3937	Lead acetate	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/kg bw/d	GRO	GRO	BDWT	WO	200	--	Selected for use in TRV development	19.2	--	3.3	--
Zmudski	1983	3940	Lead acetate	Cattle (<i>Bos taurus</i>)	4	0/2.7/5.0/20	mg/kg bw/d	MOR	MOR	MOR	WO	--	2.70	Selected for use in TRV development	--	49.49	--	19

* See reference section of text for corresponding reference

-- = Not applicable, not available

% in diet = percent in diet

% in water = percent in water

BDWT = body weight

Conc = concentration

EM = embryo

g/L = grams per liter

GRO = growth

LOAEL = lowest-observed adverse effects level

mg/kg bw = milligrams per kilogram of body weight

mg/kg bw/d = milligrams per kilogram of body weight per day

mg/kg diet = milligrams per kilogram of diet

mg/L = milligrams per liter

mg/ml = milligrams per milliliter

mg/org = milligrams per organism

mg/org/d = milligrams per organism per day

MOR = mortality

NOAEL = no-observed adverse effects level

PRFM = pregnant females in a population

PROG = progeny counts/numbers

PRWT = progeny weight

REP = reproduction

RHIS = reproductive organ histology

RSUC = reproductive success (general)

SURV = survival

TE = testes

TEDG = testes degeneration

TRV = Toxicity Reference Value

µg/g = micrograms per gram

µg/g bw/d = micrograms per gram of body weight per day

µg/org/d = micrograms per organism per day

WO = whole organism

ww = wet weight

Table 5.
Summary of References Evaluated to Develop Tissue TRVs for Zinc

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Dose s	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Response Site	Study NOAEL	Study LOAEL	Kidney NOAEL (µg/g, ww)	Kidney LOAEL (µg/g, ww)	Liver NOAEL (µg/g, ww)	Liver LOAEL (µg/g, ww)
Agarwal	1986	21084	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	--	--	--	--
Alaoui	1985	36854	Zinc acetate	Rat (<i>Rattus norvegicus</i>)	2	0/150	mg/kg diet	REP	REP	ORWT	TE	150	--	--	--	--	--
Alaoui	1985	36854	Zinc acetate	Rat (<i>Rattus norvegicus</i>)	2	0/150	mg/kg diet	GRO	GRO	BDWT	WO	150	--	--	--	--	--
Amemiya	1986	21069	zinc (unspecified)	Rat (<i>Rattus norvegicus</i>)	2	0/1000	ug/g	REP	REP	PRWT	WO	1000	--	36.28	--	51.3	--
Aulerich	1991	46274	Zinc sulfate heptahydrate	Mink (<i>Mustela vison</i>)	4	0/66.2/105.7/164.8	mg/kg bw/d	MOR	MOR	MOR	WO	164.8	--	93	--	100	--
Aulerich	1991	46274	Zinc sulfate heptahydrate	Mink (<i>Mustela vison</i>)	4	0/113.3/229.8/297.4	mg/kg bw/d	MOR	MOR	MOR	WO	297.4	--	31	--	51	--
Aulerich	1991	46274	Zinc sulfate heptahydrate	Mink (<i>Mustela vison</i>)	4	0/104.3/227.5/323.6	mg/kg bw/d	MOR	MOR	MOR	WO	323.6	--	35	--	67	--
Aulerich	1991	46274	Zinc sulfate heptahydrate	Mink (<i>Mustela vison</i>)	4	0/76.8/178.2/326.7	mg/kg bw/d	MOR	MOR	MOR	WO	326.7	--	111	--	134	--
Barone	1998	21042	Zinc	Rat (<i>Rattus norvegicus</i>)	2	0/1000	mg/kg diet	REP	REP	PROG	WO	--	1000	--	--	--	--
Barone	1998	21042	Zinc	Rat (<i>Rattus norvegicus</i>)	2	0/1000	mg/kg diet	GRO	GRO	BDWT	WO	--	1000	--	--	--	--
Bentley	1991	40436	Zinc carbonate	Rabbit (<i>Oryctolagus cuniculus</i>)	3	0/1000/5000	ug/g	GRO	GRO	BDWT	WO	5000	--	998	--	326	--
Brink	1959	14525	Zinc carbonate	Pig (<i>Sus scrofa</i>)	6	0/0.05/0.10/0.20/0.40/0.80	% in diet	GRO	GRO	BDWT	WO	0.1	0.2	--	--	--	1600
Brink	1959	14525	Zinc carbonate	Pig (<i>Sus scrofa</i>)	6	0/0.05/0.10/0.20/0.40/0.80	% in diet	MOR	MOR	MOR	WO	0.1	0.2	--	--	--	1600
Bui	1998	21045	Zinc	Rat (<i>Rattus norvegicus</i>)	2	0/0.09746	mg/g bw	REP	REP	PRWT	WO	0.09746	--	--	--	24.6	--
Bui	1998	21045	Zinc	Rat (<i>Rattus norvegicus</i>)	2	0/0.09746	mg/g bw	GRO	GRO	BDWT	WO	0.09746	--	--	--	24.6	--
Cerklewski	1979	37008	Zinc carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/120	mg/kg diet	REP	REP	PRWT	WO	120	--	--	--	--	--
Cerklewski	1979	37008	Zinc carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/120	mg/kg diet	GRO	GRO	BDWT	WO	120	--	--	--	--	--
Cerklewski	1976	2627	Zinc carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/200	mg/kg diet	GRO	GRO	BDWT	WO	200	--	--	--	--	--
Chu	1972	42670	Zinc	Rat (<i>Rattus norvegicus</i>)	2	0/0.4	% in diet	REP	REP	PRWT	WO	--	0.4	--	--	--	391.75
Cox	1969	42838	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	2	0/0.4	% in diet	REP	REP	PRWT	WO	--	0.4	--	36.68	--	107.8
Davies	1977	14527	Zinc sulfate	Sheep (<i>Ovis aries</i>)	2	0/2065	mg/kg diet	GRO	GRO	BDWT	WO	--	2065	--	971.8	--	--
Eisemann	1979	43242	Zinc oxide	Pig (<i>Sus scrofa</i>)	2	0/581	mg/kg diet	GRO	GRO	BDWT	WO	581	--	38.58	--	56.8	--
Elliot and Walker	1968	38623	Zinc carbonate	Pig (<i>Sus scrofa</i>)	2	0/478	mg/kg diet	GRO	GRO	BDWT	WO	478	--	--	--	--	--
Food and Drug Res. Lab	1974	42292	Zinc sulfate	Rabbit (<i>Oryctolagus cuniculus</i>)	5	0/0.6/2.8/13.0/60.0	mg/kg bw/d	REP	REP	PRFM	WO	60	--	--	--	--	--
Food and Drug Res. Lab	1974	42292	Zinc sulfate	Rabbit (<i>Oryctolagus cuniculus</i>)	5	0/0.6/2.8/13.0/60.0	mg/kg bw/d	GRO	GRO	BDWT	WO	60	--	--	--	--	--
Food and Drug Res. Lab	1974	42292	Zinc sulfate	Rabbit (<i>Oryctolagus cuniculus</i>)	5	0/0.6/2.8/13.0/60.0	mg/kg bw/d	MOR	MOR	WO	60	--	--	--	--	--	
Hill	1983	45143	Zinc oxide	Pig (<i>Sus scrofa</i>)	3	0/500/5000	mg/kg diet	REP	REP	ODVP	WO	500	5000	30	367	90	1037
Hill	1983	45143	Zinc oxide	Pig (<i>Sus scrofa</i>)	3	0/500/5000	mg/kg diet	GRO	GRO	GGRO	WO	500	5000	30	367	90	1037
Hill	1983	35659	Zinc oxide	Pig (<i>Sus scrofa</i>)	3	0/500/5000	mg/kg diet	REP	REP	RHIS	WO	5000	--	--	--	--	--
Hsu	1975	14376	Zinc oxide	Pig (<i>Sus scrofa</i>)	2	0/4000	mg/kg diet	GRO	GRO	BDWT	WO	--	4000	--	238	--	645.8
Ketcheson	1969	37837	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	3	0/0.2/0.5	% in diet	REP	REP	PRWT	WO	0.2	0.5	--	--	87.10	125.0
Ketcheson	1969	37837	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	3	0/0.2/0.5	% in diet	GRO	GRO	BDWT	WO	0.5	--	--	--	125.0	--
Khera	1979	21134	Zinc acetate	Rat (<i>Rattus norvegicus</i>)	2	0/34	mg/kg bw/d	REP	REP	PRWT	WO	34	--	--	--	--	--
Khera	1979	21134	Zinc acetate	Rat (<i>Rattus norvegicus</i>)	2	0/34	mg/kg bw/d	GRO	GRO	BDWT	WO	34	--	--	--	--	--
Llewellyn	1985	2203	Zinc carbonate	Golden hamster (<i>Mesocricetus auratus</i>)	2	0/3000	mg/kg diet	GRO	GRO	BDWT	WO	3000	--	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Rat (<i>Rattus norvegicus</i>)	4	0/23.2/234/2514	mg/kg bw/d	REP	REP	ORWT	TE	234	2514	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Mouse (<i>Mus musculus</i>)	4	0/42.7/458/4927	mg/kg bw/d	REP	REP	ORWT	TE	458	4927	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Mouse (<i>Mus musculus</i>)	4	0/46.4/479/4878	mg/kg bw/d	REP	REP	ORWT	OV	479	4878	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Rat (<i>Rattus norvegicus</i>)	4	0/24.5/243/2486	mg/kg bw/d	REP	REP	ORWT	OV	2486	--	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Rat (<i>Rattus norvegicus</i>)	4	0/23.2/234/2514	mg/kg bw/d	GRO	GRO	BDWT	WO	234	2514	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Mouse (<i>Mus musculus</i>)	4	0/42.7/458/4927	mg/kg bw/d	GRO	GRO	BDWT	WO	458	4927	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Mouse (<i>Mus musculus</i>)	4	0/46.4/479/4878	mg/kg bw/d	GRO	GRO	BDWT	WO	479	4878	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Rat (<i>Rattus norvegicus</i>)	4	0/24.5/243/2486	mg/kg bw/d	GRO	GRO	BDWT	WO	2486	--	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Mouse (<i>Mus musculus</i>)	4	0/42.7/458/4927	mg/kg bw/d	MOR	MOR	MOR	WO	458	4927	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Rat (<i>Rattus norvegicus</i>)	4	0/24.5/243/2486	mg/kg bw/d	MOR	MOR	MOR	WO	2486	--	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Rat (<i>Rattus norvegicus</i>)	4	0/23.2/234/2514	mg/kg bw/d	MOR	MOR	MOR	WO	2514	--	--	--	--	--
Maita	1981	43680	Zinc sulfate heptahydrate	Mouse (<i>Mus musculus</i>)	4	0/46.4/479/4878	mg/kg bw/d	MOR	MOR	MOR	WO	4878	--	--	--	--	--
Miller	1989	14685	Zinc sulfate	Cattle (<i>Bos taurus</i>)	3	0/1000/2000	mg/kg diet	REP	REP	PRWT	WO	1000					

Table 5.
Summary of References Evaluated to Develop Tissue TRVs for Zinc

Primary Author	Year	Reference ID*	Chemical Form	Test Species	# of Conc/Dose s	Conc/Doses	Conc/Dose Units	General Effect Group	Effect Type	Effect Measure	Respon se Site	Study NOAEL	Study LOAEL	Kidney NOAEL ($\mu\text{g/g, ww}$)	Kidney LOAEL ($\mu\text{g/g, ww}$)	Liver NOAEL ($\mu\text{g/g, ww}$)	Liver LOAEL ($\mu\text{g/g, ww}$)
Schell	1996	42234	Zinc oxide	Pig (<i>Sus scrofa</i>)	4	0/236/572/762	mg/d	GRO	BDWT	WO	762	--	42.3	--	285.3	--	
Schell	1996	42234	Zinc sulfate	Pig (<i>Sus scrofa</i>)	4	0/218/624/830	mg/d	GRO	BDWT	WO	830	--	58.8	--	470.8	--	
Schlicker	1968	25	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	2	0/0.2	% in diet	REP	REP	PRWT	WO	0.2	--	--	21.5	--	
Schlicker	1968	25	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	2	0/0.4	% in diet	REP	REP	PRWT	WO	--	0.4	--	--	187.1	
Schlicker	1968	25	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	2	0/0.4	% in diet	GRO	GRO	BDWT	WO	--	0.4	--	--	187.1	
Scott	1979	43264	Zinc carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/0.75	% in diet	GRO	GRO	BDWT	WO	--	0.75	--	--	131	
Settemire	1967	113	Zinc chloride	Mouse (<i>Mus musculus</i>)	2	0/150	mg/kg/d	REP	REP	PRWT	NR	150	--	97.3	--	128	--
Settemire	1967	113	Zinc chloride	Mouse (<i>Mus musculus</i>)	2	0/150	mg/kg/d	MOR	MOR	MOR	WO	150	--	97.3	--	128	--
Shankar	1986	46830	Zinc oxide	Rat (<i>Rattus norvegicus</i>)	2	0/400	mg/kg diet	GRO	GRO	BDWT	WO	400	--	27.78	--	32.17	--
Urabe	1990	40997	Zinc carbonate	Rat (<i>Rattus norvegicus</i>)	2	0/30	mg/g diet	GRO	GRO	BDWT	WO	30	--	--	--	--	--
Van der Schee	1980	21171	Zinc sulfate heptahydrate	Sheep (<i>Ovis aries</i>)	3	0/223/409	mg/kg diet	MOR	MOR	MOR	WO	409	--	20	--	30.3	--
Wapnir	1993	39821	Zinc sulfate	Rat (<i>Rattus norvegicus</i>)	2	0/0.44	g/kg diet	GRO	GRO	BDWT	WO	0.44	--	--	--	--	--
Willoughby	1972	14385	Zinc oxide	Horse (<i>Equus caballus</i>)	2	0/5400	mg/kg diet	MOR	MOR	MOR	WO	5400	--	--	--	--	--
Zhang	1995	39356	Zinc oxide	Mouse (<i>Mus musculus</i>)	2	0/6010	mg/kg diet	GRO	GRO	BDWT	WO	6010	--	--	--	44.2	--
Zhang	1995	39356	Zinc sulfate	Mouse (<i>Mus musculus</i>)	2	0/6075	mg/kg diet	GRO	GRO	BDWT	WO	6075	--	--	--	52	--
Zhang	1995	39356	Zinc methionine	Mouse (<i>Mus musculus</i>)	2	0/6135	mg/kg diet	GRO	GRO	BDWT	WO	6135	--	--	--	44.2	--

* See reference section of text for corresponding reference

-- = Not applicable, not available

% in diet = percent in diet

BDWT = body weight

Conc = concentration

g/kg diet = grams per kilogram of diet

GGRO = general growth

GREP =

GRO = growth

LOAEL = lowest-observed adverse effects level

mg/d = milligrams per day

mg/g diet = milligrams per gram of diet

mg/kg/d = milligrams per kilogram per day

mg/kg bw/d = milligrams per kilogram of body weight per day

mg/kg diet = milligrams per kilogram of diet

MOR = mortality

NOAEL = no-observed adverse effects level

NR = not reported

ODVP = offspring development

OV = ovulation rate

PRFM = pregnant females in a population

PROG = progeny counts/numbers

PRWT = progeny weight

REP = reproduction

RHIS = reproductive organ histology

TE = testes

TRV = Toxicity Reference Value

$\mu\text{g/g}$ = micrograms per gram

WO = whole organism

ww = wet weight